

What is claimed is:

1. A method for isotopically labeling a functional group possessed by an amino acid residue of a protein, comprising the step of reacting an enzyme with the protein in the presence of an isotope-labeling compound.
- 5 2. The method of claim 1, wherein the enzyme is a transferase.
3. The method of claim 1, wherein the enzyme is a transglutaminase, the amino acid residue is a glutamine residue and the isotope-labeling compound is an ammonium salt.
4. The method of claim 1, wherein the enzyme is a transglutaminase, the  
10 amino acid residue is a glutamine residue, the functional group is  $\gamma$ -carboxamido group and the isotope-labeling compound is an ammonium salt.
5. The method of claim 3, wherein the transglutaminase is calcium-independent.
6. The method of claim 3, wherein the transglutaminase is calcium-  
15 dependent and the reaction of the transglutaminase with the protein is conducted in the presence of calcium.
7. The method of claim 3, wherein the transglutaminase is reacted with a protein in an aquatic environment at the pH of about pH5.0 to pH9.0 and the temperature of 4°C to 55°C for about 30 seconds to about 2 days.
- 20 8. The method of claim 3, wherein the ratio of the concentration of the ammonium salt to the concentration of the protein to be labeled is more than about 10.
9. The method of claim 8, wherein the concentration of the protein to be labeled is about 1 $\mu$ M to about 40mM and the concentration of the ammonium  
25 salt is about 10 $\mu$ M to about 10M.

10. A protein whose amino acid residue has a functional group isotopically labeled according to the method of claim 1.

11. A protein whose glutamine residue has a functional group isotopically labeled according to the method of claim 3.

5 12. A method of determining the substrate specificity of a transglutaminase, which comprises the steps of

(i) reacting the transglutaminase with a protein in the presence of an isotopically labeled ammonium salt, and

10 (ii) detecting glutamine residues in the protein which are isotopically labeled by step (i).

13. The method of claim 12, wherein the transglutaminase is reacted with proteins under aquatic environment at the pH of about pH5.0 to pH9.0 and the temperature of 4°C to 55°C for about 30 seconds to about 2 days.

15 14. The method of claim 12, wherein the concentration of the ammonium salt to the concentration of the protein to be labeled is more than about 10.

15. The method of claim 14, wherein the concentration of the protein to be labeled is about 1μM to about 40mM and the concentration of the ammonium salt is about 10μM to about 10M.